

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Status of the Claims

Claim 28 is withdrawn from consideration by the Examiner because this claim is allegedly drawn to non-elected subject matter. This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, is presented, with an appropriate defined status identifier. Upon entry of this amendment, claims 26-27 and 29-30 are pending in this application. Claims 26 and 30 are currently amended. Support for the amendments is found at, for example, page 4, lines 6 and 23, and page 14, line 36.

Election/Restriction

Claim 28, which was amended in the Amendment filed on April 14, 2004, was withdrawn by the Examiner as allegedly directed to non-elected subject matter. Applicants reserve the right to pursue the subject matter of claim 28 in one or more divisional applications.

Sequence Requirements

The Office Action asserts that the application does not comply with the requirements of 37 C.F.R. §§ 1.821 through 1.825 because the specification does not contain sequence identifiers in all locations where sequences are disclosed.

The specification was amended to include sequence identification numbers on May 20, 2002. Copies of the May 20, 2002, Amendment and the Statement to Support Filing and Submission in Accordance with 37 C.F.R. §§ 1.821.-1.825 are enclosed for the Examiner's convenience.

Applicants respectfully request withdrawal of this rejection.

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Withdrawal of Prior Rejections

Applicants would like to thank the Examiner for withdrawal of the rejection of claims 26-27 under 35 U.S.C. § 101 and claims 26-27 and 29-30 under 35 U.S.C. § 102(b) over Liabeuf.

Rejection of claims 26-27 and 29-30 under 35 U.S.C. § 112, second paragraph

Claims 26-27 and 29-30 remain rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite because the term “cryptic epitope” is unclear. Specifically, the Office Action asserts that “[i]t is not stated in the claim what the cryptic epitope is.” Office Action at page 4. The Office Action further states that the “[w]hile a sequence comprising the epitope is recited, it is not clear when it is seen.” *Id.* Applicants respectfully traverse this rejection.

There is no requirement that the claim itself must provide a detailed explanation of a claim term, so long as the term can be understood by one of skill in the art considering the usage of the term within the claim and the support and the specification. A claim is not indefinite merely because it poses an issue of claim construction. *Exxon Research and Engineering Co. v. United States*, 265 F.3d 1371, 1375, 60 USPQ2d 1272, 1276 (Fed. Cir. 2001). A claim is definite if it is amenable to construction, however confusing that task may be. *Exxon*, 265 F.3d at 1375, 60 USPQ2d at 1276. In other words, if the meaning of the claim is discernible, the claim avoids a rejection on indefiniteness grounds. *Id.*

The specification clearly describes a cryptic epitope as well as when the cryptic epitope of the claims is revealed. For example, the specification states:

“Cryptic epitope” is intended to designate an epitope of a cellular determinant of the host which is hidden or modified and is therefore recognized as being foreign by the immune system and does not therefore produce an autoimmune reaction with destruction of the corresponding determinant and which can be used for vaccination.

The cryptic epitope should obviously be exposed, that is to say be accessible and recognized by the immune system when it is carried away by the infectious agent (in the event that

it should remain cryptic, the vaccination would not be possible).

Page 3, lines 21-32

The specification further states that “it is only possible to carry out such a vaccination with a cryptic epitope only when it is carried away by the extracellular infectious agent, or an epitope which is nonimmunogenic in its natural presentation by the cell and which is modified when it is presented at the surface of the virion.” Finally, with respect to the instant cryptic epitopes, the specification states “it has been possible to demonstrate that β_2 -microglobulin has several cryptic epitopes, which are exposed during multiplication of the HIV virus and its passage outside the cell.” Page 2, lines 33-36.

Because the meaning of the term “cryptic epitope” is discernible, claims 26-27 and 29-30 avoid a rejection on indefiniteness grounds. Accordingly, the rejection of claims 26-27 and 29-30 should be withdrawn.

Rejection of claims 26-27 and 29-30 under 35 U.S.C. § 112, first paragraph

Claims 26-27 and 29-30 are newly rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. Specifically, the Office Action states that the “claims are drawn to any antibody that binds the recited motif.”

The evidence and explanation of record do not establish that claims 26-27 and 29-30 lack written description support in the specification. The written description requirement can be satisfied by characterization of an antibody by its binding affinity provided that the applicant disclosed a “fully characterized antigen,” either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository.” *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004) (*emphasis added*) quoting “Synopsis of Application of Written Description Guidelines” from the U.S.P.T.O. Here, the antigen is fully characterized because the claims are drawn to an antibody that binds to a “recited motif,” as noted by the Office Action. Accordingly, the claims satisfy the written description requirement and no deposit is necessary.

Applicants respectfully request withdrawal of the rejection of claims 26-27 and 29-30.

Rejection of claim 30 under 35 U.S.C. § 101

Claim 30 is newly rejected under 35 U.S.C. § 101 because the claim allegedly reads on a product of nature. The current form of the claim obviates this rejection. Applicants respectfully request withdrawal of this rejection.

Rejection of Claims 26-27 and 29-30 under 35 U.S.C. § 102(b)

Claims 26-27 and 29-30 are newly rejected under 35 U.S.C. § 102(b) over Arthur *et al.*, *Science* 258:1935, in view of Galea *et al.*, *Vaccine* 17:1700. The present form of the claims obviates this rejection. Applicants respectfully request withdrawal of this rejection.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date Jan. 13, 2004

By 

FOLEY & LARDNER LLP

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Stephen B. Maebius

Attorney for Applicant

Registration No. 35,264

Amy M. Rocklin

Attorney for Applicant

Registration No. 47,033

Docket No. 065691/0216

Receipt is hereby acknowledged of the following:

Applicants: Jean-Claude Chermann et al.

Serial No.: 09/827,345

Filing Date: April 6, 2001

For: VACCINE AGAINST INFECTIOUS AGENTS HAVING AN INTRACELLULAR
PHASE; COMPOSITION FOR THE TREATMENT AND PREVENTION OF HIV
INFECTIONS, ANTIBODIES AND METHOD OF DIAGNOSIS

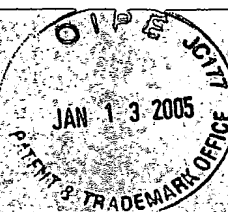
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2. Petition for Extension of Time for 2 months
3. Preliminary Amendment
4. Statement to Support Filing and Sequence Listing (hard copy and disk) copy of Notice to Comply

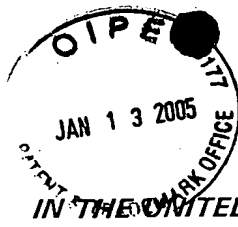
Date Due: June 8, 2002

Date: May 20, 2002

Return to: SBM/mk

Inspected by: *Bm*





Atty. Dkt. No 065691-0216

Applicant: Jean-Claude CHERMANN et al.
Title: VACCINE AGAINST INFECTIOUS AGENTS HAVING AN INTRACELLULAR
PHASE, COMPOSITION FOR THE TREATMENT AND PREVENTION OF
HIV INFECTIONS, ANTIBODIES AND METHOD OF DIAGNOSIS
Appl. No.: 09/827,345
Filing Date: 04/06/2001
Examiner: Unknown
Art Unit: 1648

PETITION FOR EXTENSION OF TIME

Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicant hereby petitions the Commissioner under 37 C.F.R. §1.136(a) for a two-month extension of time for response in the above-identified application for the period required to make the attached response timely.

The extension fee for response within the second month is \$400.00. A check for this amount is enclosed herewith.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

Respectfully submitted,

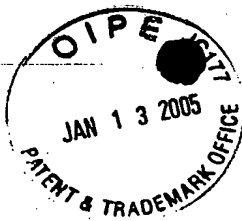
Date May 20, 2002

FOLEY & LARDNER
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By Phillip J. Antuola

for / Stephen B. Maebius
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Registration No. 35,264

Reg. No.
38,819



Atty. Dkt. No. 065691-0216

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Jean-Claude CHERMANN et al.

Title: VACCINE AGAINST INFECTIOUS AGENTS HAVING AN INTRACELLULAR PHASE, COMPOSITION FOR THE TREATMENT AND PREVENTION OF HIV INFECTIONS, ANTIBODIES AND METHOD OF DIAGNOSIS

Appl. No.: 09/827,345

Filing Date: 04/06/2001

Examiner: Unknown

Art Unit: 1648

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination of the present Application, Applicants respectfully request that the above-identified prior application be amended as follows:

In the Specification:

Please amend the specification as follows:

On page 4, delete the 2nd and 3rd paragraphs and replace these paragraphs with the following in accordance with 37 CFR § 1.121. A marked up version showing changes is attached.

The peptides according to the present invention are the following:

01-P1 IQRTPKIQVYSRHPA (SEQ ID NO: 1)

(Ile-Gln-Arg-Thr-Pro-Lys-Ile-Gln-Val-Tyr-Ser-Arg-His-Pro-Ala)

02-P4 FHPSDIEVDLLKDGE (SEQ ID NO: 2)

(Phe-His-Pro-Ser-Asp-Ile-Glu-Val-Asp-Leu-Leu-Lys-Asp-Gly-Glu)

03-P9 ACRVNHVTLSQLKIV (SEQ ID NO: 3)

(Ala-Cys-Arg-Val-Asn-His-Val-Thr-Leu-Ser-Gln-Pro-Lys-Ile-Val)

It is also possible to use a smaller part (7 amino acids) of these 15 amino acids which lifts the neutralization of the virus by the monoclonal antibodies B1G6 or B2G2.2:

04-R-7-V RTPKIQV (SEQ ID NO: 4) (Arg-Thr-Pro-Lys-Ile-Gln-Val)

05-S-7-K SQPKIVK (SEQ ID NO: 5) (Ser-Gln-Pro-Lys-Ile-Val-Lys)

06-F-7-E FHPSDIE (SEQ ID NO: 6) (Phe-His-Pro-Ser-Asp-Ile-Glu)

On pages 4 and 5, delete the bridging paragraph and replace this paragraph with the following in accordance with 37 CFR § 1.121. A marked up version showing changes is attached.

A common structure PKI (3 amino acids) appears to be the unit which is responsible; hence the following amino acid modifications:

07-TLSRTPKIQV (SEQ ID NO: 7) (Thr-Leu-Ser-Arg-Thr-Pro-Lys-Ile-Gln-Val) No. 185

08-IYLTQPKIKV (SEQ ID NO: 8) (Ile-Tyr-Leu-Thr-Gln-Pro-Lys-Ile-Lys-Val) No. 186

09-IQRTPKIQVY (SEQ ID NO: 9) (Ile-Gln-Arg-Thr-Pro-Lys-Ile-Gln-Val-Tyr) No. 187

10-TLSQPKIVKN (SEQ ID NO: 10) (Thr-Leu-Ser-Gln-Pro-Lys-Ile-Val-Lys-Asn) No. 188

11-IQRTQIVKW (SEQ ID NO: 11) (Ile-Gln-Arg-Thr-Pro-Gln-Ile-Val-Lys-Trp) No. 189

12-IQRTPNIVKW (SEQ ID NO: 12) (Ile-Gln-Arg-Thr-Pro-Asn-Ile-Val-Lys-Trp) No. 190

On page 5, delete the 1st, 2nd, and 3rd full paragraphs and replace these paragraphs with the following in accordance with 37 CFR § 1.121. A marked up version showing changes is attached.

It is also possible to introduce a cysteine and a glycosylation site:

13-CYNPSDIE (SEQ ID NO: 13) (Cys-Tyr-Asn-Pro-Ser-Asp-Ile-Glu)

- 14-YCNPEST (SEQ ID NO: 14) (Tyr-Cys-Asn-Pro-Glu-Ser-Thr)
- 15-NFLNCYVS (SEQ ID NO: 15) (Asn-Phe-Leu-Asn-Cys-Tyr-Val-Ser)
- 16-LNCYVSPSD (SEQ ID NO: 16) (Leu-Asn-Cys-Tyr-Val-Ser-Pro-Ser-Asp)

Finally, it is possible to use the peptides using the different variations according to the species (mice, primates, rabbits, guinea pigs):

- 17-KTPQIQV (SEQ ID NO: 17) (Lys-Thr-Pro-Gln-Ile-Gln-Val)
- 18-FHPPQIE (SEQ ID NO: 18) (Phe-His-Pro-Pro-Gln-Ile-Glu)
- 19-FHPPHIE (SEQ ID NO: 19) (Phe-His-Pro-Pro-His-Ile-Glu)
- 20-AEPKTVY (SEQ ID NO: 20) (Ala-Glu-Pro-Lys-Thr-Val-Tyr)
- 21-SQPKTVY (SEQ ID NO: 21) (Ser-Gln-Pro-Lys-Thr-Val-Tyr)
- 22-ILSRTPKIQV (SEQ ID NO: 22) (Ile-Leu-Ser-Arg-Thr-Pro-Lys-Ile-Gln-Val)

These peptides of SEQ ID NOS. 1 to 22 contain only the preferential choice; it is possible, as has been indicated above, to find equivalent peptides.

On page 6, delete the 2nd full paragraph and replace this paragraph with the following in accordance with 37 CFR § 1.121. A marked up version showing changes is attached.

Analysis of the structure of the regions selected for P1, P9 and P10 can be carried out by methods such as the selection using alanine to replace each amino acid separately, particularly in the RTPKIQV (SEQ ID NO: 4) region, in order to determine the possible amino acids. It is also possible to use techniques using biotinylation of each peptide, followed by selection by EIA with the antibodies in order to determine the loss of attachment.

On page 13, delete the 3rd full paragraph and replace this paragraph with the following in accordance with 37 CFR § 1.121. A marked up version showing changes is attached.

The peptide R7V (RTPKIQV) (SEQ ID NO: 4) was extended by 2 amino acids in order to allow the coupling. The structure used as immunogen is RTPKIQVGY (SEQ ID NO: 23).

On pages 15-16, delete the bridging paragraph and replace this paragraph with the following in accordance with 37 CFR § 1.121. A marked up version showing changes is attached.

Methods

Chimeric recombinant viruses were constructed by PCR-directed mutagenesis. Two constructs based on the R7V sequence and HIV-1 LAV were obtained, in which seven amino acids of the V3 region of gp120 have been replaced by the R7V sequence. The positions of the mutated sequences are shown in the following table: (SEQ ID NOS 24, 4 and 4, respectively in order of appearance).

HIV-1 LAV (V3)	NNNTRKSIRIQRGPGRAFVT		
R7V	RTPKIQV	(1)	RPL
R7V	RTPKIQV	(2)	PLG

The EcoRI₅₂₋₇₈-XhoI₈₄₀₁ fragment of HIV-1 LAV cloned into the vector Bluescript was used as template for subsequent constructs. In the first stage, the DNA fragments flanked by primers containing the BglII restriction site at one end and the nucleotide sequence encoding R7V at the other end were synthesized for the RPL and PLG constructs by PCR amplification. The mutagenesis oligonucleotides used consisted of a (+) primer ACACCAAAGATACAAGTTGTTACAAATAGGAAAA (SEQ ID NO: 25) and a (-) primer TTGTATCTTTGGTGTCTCTGGATCCGGATACTTT (SEQ ID NO: 26) for the RPL construct and of a (+) primer CGTACACCAAAAATCCAGGTCCAGAGAGGACCA (SEQ ID NO: 27) and a (-) primer GATTTTTGGTGTACGCGTATTGTTGTTGGGTCT (SEQ ID NO: 28) for the PLG construct. In the second stage, two PCR products for each construct were mixed and amplified using the primers containing the BglII restriction sites. The RPL and PLG fragments were cleaved by the enzyme BglII and inserted into the vector Bluescript containing the EcoRI₅₂₇₈-XhoI₈₄₀₁ fragment of HIV-1 LAV, cleaved by BglII. In addition to the R7V sequence, the amplification primers contained modifications in the nucleotide sequence leading to the appearance of new BamHI and MluI restriction sites in the RPL and PLG constructs respectively, without additional modifications in the amino acid sequence. The new restriction sites were used to screen the mutated sequences. Finally, the EcoRI₅₂₇₈-XhoI₈₄₀₁ fragments of HIV-1 LAV containing the RPL and PLG constructs were inserted into the plasmid pNL4-3 by

homologous recombination using the EcoRI and XhoI restriction sites. The constructs were checked by restriction enzyme analysis.

REMARKS

The specification has been amended to include sequence identification numbers.
No new matter has been added.

Respectfully submitted,

Date May 20, 2002

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By Phillip J. Artiola ^{Reg. No.} 38,819

for / Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Marked up rewritten paragraphs:

On page 4, 2nd and 3rd paragraphs:

The peptides according to the present invention are the following:

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screen the mutated sequences. Finally, the EcoRI₅₂₇₈-XhoI₈₄₀₁ fragments of HIV-1 LAV containing the RPL and PLG constructs were inserted into the plasmid pNL4-3 by homologous recombination using the EcoRI and XhoI restriction sites. The constructs were checked by restriction enzyme analysis.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket No: 065691-0216

In re patent application of
CHERMANN, JEAN-CLAUDE et al.

Serial No. 09/827,345

Filed: April 6, 2001

For: VACCINE AGAINST INFECTIOUS AGENTS HAVING AN INTRACELLULAR PHASE,
COMPOSITION FOR THE TREATMENT AND PREVENTION OF HIV INFECTIONS,
ANTIBODIES AND METHOD OF DIAGNOSIS



STATEMENT TO SUPPORT FILING AND SUBMISSION IN
ACCORDANCE WITH 37 C.F.R. §§ 1.821-1.825

Assistant Commissioner for Patents
Washington, D.C. 20231
Box SEQUENCE

Sir:

In connection with a Sequence Listing submitted concurrently
herewith, the undersigned hereby states that:

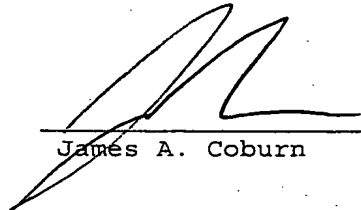
1. the submission, filed herewith in accordance with 37
C.F.R. § 1.821(g), does not include new matter;
2. the content of the attached paper copy and the
attached computer readable copy of the Sequence Listing, submitted in
accordance with 37 C.F.R. § 1.821(c) and (e), respectively, are the same;
and
3. all statements made herein of their own knowledge are
true and that all statements made on information and belief are believed to
be true; and further, that these statements were made with the knowledge
that willful false statements and the like so made are punishable by fine
or imprisonment, or both, under Section 1001 of Title 18 of the United

Serial No. 09/827,345

States Code and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

Respectfully submitted,

March 28, 2008
Date


James A. Coburn

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SEQUENCE LISTING

<110> CHERMANN, JEAN-CLAUDE
LE CONTEL, CAROLE
GALEA, PASCALE

<120> VACCINE AGAINST INFECTIOUS AGENTS HAVING AN
INTRACELLULAR PHASE, COMPOSITION FOR THE TREATMENT AND
PREVENTION OF HIV INFECTIONS, ANTIBODIES AND METHOD OF
DIAGNOSIS

<130> 065691-0216

<140> 09/827,345

<141> 2001-04-06

<150> 09/599,549

<151> 2000-06-23

<150> PCT/FR96/01006

<151> 1996-06-28

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<170> PatentIn Ver. 2.1

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<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic
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1 5 10

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<210> 21

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Ala Phe Val Thr
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35

<210> 27

<211> 33

<212> DNA

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33

<210> 28
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33

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